

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:

Fischetti, et al.

Serial No. continuation of 09/671,880

Group: 1616

Filed: September 28, 2000

Examiner: Raj Bawa, Ph.D.

For: A Composition Incorporating Bacterial Phage Associated Lysing Enzymes for Treating Dermatological Infections

The Honorable Commissioner of
Patents and Trademarks
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

First, please note that all correspondence should go to the address of the undersigned attorney, said address being:

2120 L Street, N.W.
Suite 210
Washington, D.C. 20037

IN THE TITLE

Please cancel the title and replace it with the following:

--THERAPEUTIC TREATMENT OF UPPER RESPIRATORY INFECTIONS--

IN THE SPECIFICATION

Page 1, after the title, line 5, please change the following:

The following application is a continuation of 09/671,880 which is a continuation -

in - part of 09/497,495 filed April 18, 2000, now U.S. Patent No. 6,238,661, which is a continuation 09/395,636 filed September 14, [2000] 1999, now U.S. Patent No. 6,056,954 which is continuation-in-part of U.S. Patent Application 08/962,523, filed October 31, 1997, now U.S. Patent No. 5,997,862.

Page 1, the paragraph containing lines 21-22 and beginning at line 20 should be changed as follows:

In the past, antibiotics have been used to treat various infections. The work of Selman Waksman in the introduction and production of Streptomyces[,] and Dr. Fleming's discovery of penicillin, [are well known] as well as the work of numerous others in the field of antibiotics , are well known. Over the years, there have been additions and chemical modifications to the "basic" antibiotics in attempts to make them more powerful, or to treat people allergic to these antibiotics.

Page 2, the paragraph containing line 2 and beginning at line 1 should be changed as follows:.

Others have found new uses for these antibiotics. U.S. Patent No. 5,260,292 (Robinson et al.) discloses [the] a topical treatment of acne with aminopenicillins. The method and composition for topically treating acne and acneiform dermal disorders includes applying an amount of an antibiotic selected from the group consisting of ampicillin, amoxicillin, other aminopenicillins, and cephalosporins, and derivatives and analogs thereof, effective to treat the acne and acneiform dermal disorders. U.S. Patent No. 5,409,917 (Robinson et al.) discloses the topical treatment of acne with cephalosporins.

Page 2, the paragraph containing lines 15 and 16 and beginning at line 8 should be changed as follows:

However, as more antibiotics have been prescribed or used at an ever increasing rate for a variety of illnesses, increasing numbers of bacteria have developed a resistance to antibiotics. Larger doses of stronger antibiotics are now being used to treat ever more resistant strains of bacteria. Multiple antibiotic resistant bacteria have consequently developed. The use of more antibiotics and the number of bacteria showing resistance has led to increasing the amount of time that the antibiotics need to be used. Broad, non-specific antibiotics, some of which have detrimental effects on the patient, are now being used more frequently. Also, antibiotics do not easily penetrate mucus linings. Additionally, the number of people allergic to antibiotics appears to be increasing.

[Additionally, the number of people allergic to antibiotics appears to be increasing.]

The paragraph on page 2, beginning at line 18, should be changed as follows::

Attempts have been made to treat bacterial diseases [with] by the use of bacteriophages. U.S. Patent No. 5,688,501 (Merril, et al.) discloses a method for treating an infectious disease caused by bacteria in an animal with lytic or non-lytic bacteriophages that are specific for particular bacteria.

Page 3, please change the paragraph containing line 4, and beginning at line 2, as follow:

It is to be noted that the direct introduction of bacteriophages into an animal to prevent or fight diseases has certain drawbacks. Specifically, the bacteria must be in the right growth phase for the phage to attach. Both the bacteria and the [and the] phage have to be in the correct and synchronized growth cycles. Additionally, there must be the right number of phages to attach to the bacteria; if there are too many or too few phages, there will either be no attachment or no production of the lysing enzyme. The phage must also be active enough. The phages are also inhibited by many things including bacterial debris from the organism it is going to attack. Further complicating the direct use of bacteriophage to treat bacterial infections is the possibility of immunological reactions, rendering the phage non-functional.

Page 3, please change the paragraph containing (and beginning at) line 11 to:

Consequently, others have explored the use [other] of safer and more effective means to treat and prevent bacterial infections.

Page 3, please change the paragraph containing line 14 and beginning at line 13 to: :

U.S. Patent No. 5,604,109 (Fischetti et al.) relates to the rapid detection of Group A [streptococci] Streptococci in clinical specimens, through the enzymatic digestion by a semi-purified Group C streptococcal phage associated lysin enzyme. The lytic enzyme of this patent is used in U.S. Patent No. 5,997,862 (Fischetti, et. al.), U.S. Patent No. 5,985,271, (Fischetti et al.) and U.S. Patent No. 6,017,528(Fischetti et al.) which disclose the use of an oral delivery mode, such as a

candy, chewing gum, lozenge, troche, tablet, a powder, an aerosol, a liquid or a liquid spray, containing a lysin enzyme produced by group C streptococcal bacteria infected with a C1 bacteriophage for the prophylactic and therapeutic treatment of Streptococcal A throat infections, commonly known as strep throat.

Page 4, please change the paragraph containing line 8 and beginning at line 6 to—

The method for obtaining and purifying the lytic enzyme produced by a bacteria infected with the bacteriophage is known in the art. Some recent evidence suggests that the phage enzyme that lyses the [streptococcus] *Streptococcus* organism may actually be a bacterial enzyme that is used to construct the cell wall and the phage. While replicating in the bacterium, a phage gene product may cause the upregulation or derepression of bacterial enzyme for the purpose of releasing the bacteriophage. These bacterial enzymes may be tightly regulated by the bacterial cell and are used by the bacteria for the construction and assembly of the cell wall.

Page 5, please change the paragraph beginning at line 18 to:

In one embodiment of the invention, the prophylactic and therapeutic treatment of a variety of illnesses caused by *Streptococcal pneumoniae*, *Streptococcus fasciae*, and *Hemophilus influenza* are disclosed. In another embodiment of the invention, gram negative bacterial infections caused by *Listeria*, *Salmonella*, *E. coli*, and *Campylobacter*, are treated by the use of lytic enzymes. These and other bacteria, which can infect the digestive system, can be treated by incorporating the lytic

enzymes in suppository enemas, in syrups, or in other carriers to [get] go directly to the site of the infection(s).

Page 6, please change the paragraph beginning at line 7 to

Vaginal infections caused by Group B *Streptococcus* can cause premature [birth] births and subsequent complications resulting in neonatal sepsis. Lysin incorporated into tampons specific for group B strep would prevent [infection] infections of the neonate during birth without disturbing normal vaginal flora so that women would not be overcome by yeast infection as a result of antibiotic therapy.

Page 6, the paragraph containing and beginning at line 12 should be changed to:

In another embodiment of the invention, eye drops containing lytic enzymes of [Hemophilus] Hemophilus, *Pseudomonas*, and/or *Staphylococcus* can be used to directly treat eye infections. Treatment with lytic enzymes are faster and more expedient than with antibiotics.

Page 6, the paragraph containing line 21 and beginning at line 18 should be changed to:

In another embodiment of the invention the lytic enzyme is administered in the form of a candy, chewing gum, lozenge, troche, tablet, a powder, an aerosol, a liquid, a liquid spray, or toothpaste for the prevention or treatment of bacterial infections associated with upper respiratory

tract illnesses[.]

Page 7, the paragraph containing line 4 and beginning at line 1 should be changed to:

In another embodiment of the invention, species specific lytic enzymes can be used in the treatment of bacterial infections associated with topical or dermatological infections, administered in the form of a topical ointment or cream. In another embodiment of the invention, the lytic enzyme would be administered in an aqueous form. In yet another embodiment of the invention, lysostaphin, the enzyme which lyses [Staphylococcus aureus] *Staphylococcus aureus*, can be included in the therapeutic agent. In a further embodiment of the invention, conventional antibiotics may be included in the therapeutic agent with the lytic enzyme, and with or without the presence of lysostaphin. More than one lytic enzyme may also be included in the prophylactic or therapeutic agent.

Page 7, the paragraph beginning at line 14, and containing line 17 should be changed to:

The method for treating bacterial infections comprises treating the infection with a therapeutic agent comprising an effective amount of at least one lytic enzyme produced by a bacteria infected with a bacteriophage specific for the bacteria. [The] The lytic enzyme is preferably in an environment having a pH which allows for activity of [said] the lytic enzyme.

Page 7, the paragraph containing line 20 and beginning at line 18 should be changed to:

The lytic enzyme can be used for the treatment or prevention of *Hemophilus* [influenza] *influenza*, *Pseudomonas*, *Streptococcus pneumoniae*, *Streptococcus fasciae*, *Streptococcus* group B, *Listeria*, *Salmonella*, *E. coli*, *Campylobacter*, [and] other bacteria, and any combination thereof.

Page 13, the paragraph containing line 19 and beginning on line 17 should be changed to:

Another use of a lytic enzyme is for the treatment of bacterial infections of the digestive tract. The method for treating a bacterial infection of the digestive tract comprises treating the bacterial infection with a composition comprising an effective amount of at least one lytic enzyme produced by a bacteria infected with a bacteriophage specific for the bacteria, and a carrier for delivering said lytic enzyme to the digestive tract. In a preferred embodiment of the invention, the bacterial infections being treated are being caused by gram negative bacteria selected from the group consisting of *Listeria*, *Salmonella*, *E. coli*, and *Campylobacter*. However, this method and composition will effectively treat other bacteria, when the appropriate lytic enzyme is used.

Page 20, the paragraph containing line 17 should be changed to

The effective dosage rates or amounts of the lytic enzyme to treat the infection, and the duration of treatment will depend in part on the seriousness of the infection, the duration of exposure of the recipient to the infectious bacteria, the number of square centimeters of skin or tissue which are infected, the depth of the infection, the seriousness of the infection, and a variety of a number of other variables. The composition may be applied anywhere from once to several times

a day, and may be applied for a short or long term period. The usage may last for days or weeks. Any dosage form employed should provide for a minimum number of units for a minimum amount of time. The concentration of the active units of enzyme believed to provide for an effective amount or dosage of enzyme may be in the range of about 100 units/ml to about 500,000 units/ml of composition, preferably in the range of about 1000 units/ml to about 100,000 units/ml, and most preferably from about 10,000 to 100,000 units/ml. The amount of active units per ml and the duration of time of exposure depends on the nature of infection, and the amount of contact the carrier allows the lytic enzyme to have. It is to be remembered that the enzyme works best when in a fluid environment. Hence, effectiveness of the enzyme is in part related to the amount of moisture trapped by the carrier. In another preferred embodiment, a mild surfactant is present in an amount effective to potentiate the therapeutic effect of the lytic enzyme. Suitable mild surfactants include, inter alia, esters of polyoxyethylene sorbitan and fatty acids (Tween series), octylphenoxy polyethoxy ethanol (Triton-X series), n-Octyl-.beta.-D-glucopyranoside, n-Octyl-.beta.-D-thioglucopyranoside, n-Decyl-.beta.-D-glucopyranoside, n-Dodecyl-.beta.-D-glucopyranoside, and biologically occurring surfactants, e.g., fatty acids, glycerides, monoglycerides, deoxycholate and esters of deoxycholate.

Page 25, line 2, the paragraph beginning with line 1, should be changed to:

It is also to be remembered that a carrier may have more than one lytic enzyme. For instance, [A] a throat lozenge may comprise just a lysin enzyme (which lyses the *Streptococcus A* strain causing "strep" throat, or it may also include the lytic enzymes for *Hemophilus*. Similarly, the carrier for treating burns and wounds, or infections of the skin, may contain just one lytic enzyme, or a

combination of lytic enzymes, for the treatment of *Pseudomonas*, *Streptococcus*, *Staphylococcus*, or any other of a number of bacteria.

IN THE CLAIMS

Please cancel claims 1-7.

Please add the following claims

- 8) A method for treatment of a streptococcal infection, comprising:
 - administering a composition comprising an effective amount of a lysin enzyme genetically coded for by a C1 bacteriophage capable of infecting a group C Streptococcal bacteria , said lysin enzyme characterized by the ability to specifically destroy the cell wall of Group A Streptococci; and
 - a carrier for delivering said lysin enzyme to a mouth, throat, or nasal passage.
- 9. The method according to claim 8, wherein said carrier is selected from the group consisting of candy, chewing gum, lozenge, troche, tablet, powder, aerosol, liquid, liquid spray, nasal sprays and nasal ointments.
- 10. The method according to claim 8, further comprising a buffer that maintains pH of the composition at a range between about 4.0 and 9.0.
- 11. The method according to claim 10, wherein said buffer maintains the pH of the composition at range between 5.5 and 7.5.

12. The method according to claim 10, wherein said buffer comprises a reducing agent.
13. The method according to claim 12, wherein said reducing agent is dithiothreitol.
14. The method according to claim 10, wherein said buffer comprises a metal chelating agent.
15. The method according to claim 14, wherein said metal chelating agent is ethylenediaminetetraacetic disodium salt.
16. The method according to claim 10, wherein said buffer is a citrate-phosphate buffer.
17. The method according to claim 8, further comprising a bactericidal or bacteriostatic agent as a preservative.
18. The method according to claim 8, wherein said lysin enzyme is lyophilized.
19. The method according to claim 9, wherein said carrier further comprises a sweetener.
20. The method according to claim 9, wherein said carrier is a candy.

21. The method according to claim 9, wherein said carrier is a chewing gum.
22. The method according to claim 9, wherein said carrier is a lozenge.
23. The method according to claim 9, wherein said carrier is a troche.
24. The method according to claim 9, wherein said carrier is a powder.
21. The method according to claim 9, wherein said carrier is an aerosol.
22. The method according to claim 9, wherein said carrier is a liquid spray.
23. The method according to claim 9, wherein said carrier is a nasal spray.
24. The method according to claim 8, wherein said mammal is a human.
25. The method according to claim 8, wherein said carrier is suitable for delivering said lysin enzyme to the mouth and throat.
26. The method according to claim 8, wherein said carrier is suitable for delivering said lysin enzyme to the nasal passage.

27. A method for treating a streptococcal infection, comprising:

- an effective amount of a lysin enzyme genetically coded for by a bacteriophage , said lysin enzyme characterized by the ability to specifically destroy the cell wall of Group A Streptococci; and
- a carrier for delivering said lysin enzyme to a mouth, throat, or nasal passage.

28.. The method according to claim 27, wherein said carrier is selected from the group consisting of candy, chewing gum, lozenge, troche, tablet, powder, aerosol, liquid, liquid spray, nasal sprays and nasal ointments.

29.. The method according to claim 27, further comprising a buffer that maintains pH of the composition at a range between about 4.0 and 9.0.

30. The method according to claim 28, wherein said buffer maintains the pH of the composition at range between 5.5 and 7.5.

31. The method according to claim 27, wherein said lysin enzyme is lyophilized.

32. The method according to claim 27, wherein said carrier further comprises a sweetener.

33. The method according to claim 28, wherein said carrier is a candy.

34. The method according to claim 28, wherein said carrier is a chewing gum.
35. The method according to claim 28, wherein said carrier is a lozenge.
36. The method according to claim 28, wherein said carrier is a troche.
37. The method according to claim 28, wherein said carrier is a powder.
38. The method according to claim 28, wherein said carrier is an aerosol.
39. The method according to claim 28, wherein said carrier is a liquid spray.
40. The method according to claim 28, wherein said carrier is a nasal spray.
41. The method according to claim 27, wherein said mammal is a human.
42. The method according to claim 27, wherein said carrier is suitable for delivering said lysin enzyme to the mouth and throat.
43. The method according to claim 28, wherein said carrier is suitable for delivering said lysin enzyme to the nasal passage.

IN THE ABSTRACT

Please cancel the abstract and replace with the following:

The present invention relates to an oral delivery system containing a bacteriophage associated lysin enzyme for the treatment of Streptococcal A throat infections, commonly known as strep throat.

The application is now in condition for allowance. Please call the undersigned at (301) 603-9071 if you have any questions or comments. Thank you.

Very truly yours,



Jonathan E. Grant

Reg. No. 34,830

2120 L Street, N.W., Suite 210
Washington, D.C. 20037
(301) 603-9071

**APPENDIX - CLEAN COPY OF SPECIFICATION PARAGRAPHS
IN THE SPECIFICATION**

Page 1, beginning at line 5, should be changed as follows:

The following application is a continuation of 09/671,880 which is a continuation - in - part of 09/497,495 filed April 18, 2000, now U.S. Patent No. 6,238,661, which is a continuation 09/395,636 filed September 14, [2000] 1999, now U.S. Patent No. 6,056,954 which is continuation-in-part of U.S. Patent Application 08/962,523, filed October 31, 1997, now U.S. Patent No. 5,997,862.

Page 1, the paragraph containing lines 21-22 and beginning at line 20 should be changed as follows:

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selected from the group consisting of ampicillin, amoxicillin, other aminopenicillins, and cephalosporins, and derivatives and analogs thereof, effective to treat the acne and acneiform dermal disorders. U.S. Patent No. 5,409,917 (Robinson et al.) discloses the topical treatment of acne with cephalosporins.

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The paragraph on page 2, beginning on line 18, should be changed as follows::

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bacteria.

Page 3, please change the paragraph containing line 4, and beginning as line 2, as follow:

It is to be noted that the direct introduction of bacteriophages into an animal to prevent or fight diseases has certain drawbacks. Specifically, the bacteria must be in the right growth phase for the phage to attach. Both the bacteria and the phage have to be in the correct and synchronized growth cycles. Additionally, there must be the right number of phages to attach to the bacteria; if there are too many or too few phages, there will either be no attachment or no production of the lysing enzyme. The phage must also be active enough. The phages are also inhibited by many things including bacterial debris from the organism it is going to attack. Further complicating the direct use of bacteriophage to treat bacterial infections is the possibility of immunological reactions, rendering the phage non-functional.

Page 3, please change the paragraph containing (and beginning at) line 11 to:

Consequently, others have explored the use of safer and more effective means to treat and prevent bacterial infections.

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streptococci in clinical specimens, through the enzymatic digestion by a semi-purified Group C streptococcal phage associated lysin enzyme. The lytic enzyme of this patent is used in U.S. Patent No. 5,997,862 (Fischetti, et. al.), U.S. Patent No. 5,985,271, (Fischetti et al.) and U.S. Patent No. 6,017,528(Fischetti et al.) which disclose the use of an oral delivery mode, such as a candy, chewing gum, lozenge, troche, tablet, a powder, an aerosol, a liquid or a liquid spray, containing a lysin enzyme produced by group C streptococcal bacteria infected with a C1 bacteriophage for the prophylactic and therapeutic treatment of Streptococcal A throat infections, commonly known as strep throat.

Page 4, please change the paragraph containing line 8 and beginning at line 6 to—

The method for obtaining and purifying the lytic enzyme produced by a bacteria infected with the bacteriophage is known in the art. Some recent evidence suggests that the phage enzyme that lyses the *Streptococcus* organism may actually be a bacterial enzyme that is used to construct the cell wall and the phage. While replicating in the bacterium, a phage gene product may cause the upregulation or derepression of bacterial enzyme for the purpose of releasing the bacteriophage. These bacterial enzymes may be tightly regulated by the bacterial cell and are used by the bacteria for the construction and assembly of the cell wall.

Page 5, please change the paragraph beginning t line 18 to:

In one embodiment of the invention, the prophylactic and therapeutic treatment of a variety

of illnesses caused by *Streptococcal pneumoniae*, *Streptococcus fasciae*, and *Hemophilus influenza* are disclosed. In another embodiment of the invention, gram negative bacterial infections caused by *Listeria*, *Salmonella*, *E. coli*, and *Campylobacter*, are treated by the use of lytic enzymes. These and other bacteria, which can infect the digestive system, can be treated by incorporating the lytic enzymes in suppository enemas, in syrups, or in other carriers to go directly to the site of the infection(s).

Page 6, please change the paragraph beginning at line 7 to

Vaginal infections caused by Group B *Streptococcus* can cause premature births and subsequent complications resulting in neonatal sepsis. Lysin incorporated into tampons specific for group B strep would prevent infections of the neonate during birth without disturbing normal vaginal flora so that women would not be overcome by yeast infection as a result of antibiotic therapy.

Page 6, the paragraph containing and beginning at line 12 should be changed to:

In another embodiment of the invention, eye drops containing lytic enzymes of *Hemophilus*, *Pseudomonas*, and/or *Staphylococcus* can be used to directly treat eye infections. Treatment with lytic enzymes are faster and more expedient than with antibiotics.

Page 6, the paragraph containing line 21 and beginning at line 18 should be changed to:

In another embodiment of the invention the lytic enzyme is administered in the form of a candy, chewing gum, lozenge, troche, tablet, a powder, an aerosol, a liquid, a liquid spray, or toothpaste for the prevention or treatment of bacterial infections associated with upper respiratory tract illnesses.

Page 7, the paragraph containing line 4 and beginning at line 1 should be changed to:

In another embodiment of the invention, species specific lytic enzymes can be used in the treatment of bacterial infections associated with topical or dermatological infections, administered in the form of a topical ointment or cream. In another embodiment of the invention, the lytic enzyme would be administered in an aqueous form. In yet another embodiment of the invention, lysostaphin, the enzyme which lyses *Staphylococcus aureus*, can be included in the therapeutic agent. In a further embodiment of the invention, conventional antibiotics may be included in the therapeutic agent with the lytic enzyme, and with or without the presence of lysostaphin. More than one lytic enzyme may also be included in the prophylactic or therapeutic agent.

Page 7, the paragraph beginning at line 14, and containing line 17 should be changed to:

The method for treating bacterial infections comprises treating the infection with a therapeutic agent comprising an effective amount of at least one lytic enzyme produced by a bacteria infected with a bacteriophage specific for the bacteria. The lytic enzyme is preferably in an environment having a pH which allows for activity of the lytic enzyme.

Page 7, the paragraph containing line 20 and beginning at line 18 should be changed to:

The lytic enzyme can be used for the treatment or prevention of *Hemophilus influenza*, *Pseudomonas*, *Streptococcus pneumoniae*, *Streptococcus fasciae*, *Streptococcus* group B, *Listeria*, *Salmonella*, *E. coli*, *Campylobacter*, other bacteria, and any combination thereof.

Page 13, the paragraph containing line 19 and beginning on line 17 should be changed to:

Another use of a lytic enzyme is for the treatment of bacterial infections of the digestive tract. The method for treating a bacterial infection of the digestive tract comprises treating the bacterial infection with a composition comprising an effective amount of at least one lytic enzyme produced by a bacteria infected with a bacteriophage specific for the bacteria, and a carrier for delivering said lytic enzyme to the digestive tract. In a preferred embodiment of the invention, the bacterial infections being treated are being caused by gram negative bacteria selected from the group consisting of *Listeria*, *Salmonella*, *E. coli*, and *Campylobacter*. However, this method and composition will effectively treat other bacteria, when the appropriate lytic enzyme is used.

Page 20, the paragraph containing line 17 should be changed to

The effective dosage rates or amounts of the lytic enzyme to treat the infection, and the duration of treatment will depend in part on the seriousness of the infection, the duration of

exposure of the recipient to the infectious bacteria, the number of square centimeters of skin or tissue which are infected, the depth of the infection, the seriousness of the infection, and a variety of a number of other variables. The composition may be applied anywhere from once to several times a day, and may be applied for a short or long term period. The usage may last for days or weeks. Any dosage form employed should provide for a minimum number of units for a minimum amount of time. The concentration of the active units of enzyme believed to provide for an effective amount or dosage of enzyme may be in the range of about 100 units/ml to about 500,000 units/ml of composition, preferably in the range of about 1000 units/ml to about 100,000 units/ml, and most preferably from about 10,000 to 100,000 units/ml. The amount of active units per ml and the duration of time of exposure depends on the nature of infection, and the amount of contact the carrier allows the lytic enzyme to have. It is to be remembered that the enzyme works best when in a fluid environment. Hence, effectiveness of the enzyme is in part related to the amount of moisture trapped by the carrier. In another preferred embodiment, a mild surfactant is present in an amount effective to potentiate the therapeutic effect of the lytic enzyme. Suitable mild surfactants include, inter alia, esters of polyoxyethylene sorbitan and fatty acids (Tween series), octylphenoxy polyethoxy ethanol (Triton-X series), n-Octyl-.beta.-D-glucopyranoside, n-Octyl-.beta.-D-thioglucopyranoside, n-Decyl-.beta.-D-glucopyranoside, n-Dodecyl-.beta.-D-glucopyranoside, and biologically occurring surfactants, e.g., fatty acids, glycerides, monoglycerides, deoxycholate and esters of deoxycholate.

Page 25, line 2, the paragraph beginning with line 1 should be changed to:

It is also to be remembered that a carrier may have more than one lytic enzyme. For instance, a throat lozenge may comprise just a lysin enzyme (which lyses the *Streptococcus* A strain causing "strep" throat, or it may also include the lytic enzymes for *Hemophilus*. Similarly, the carrier for treating burns and wounds, or infections of the skin, may contain just one lytic enzyme, or a combination of lytic enzymes, for the treatment of *Pseudomonas*, *Streptococcus*, *Staphylococcus*, or any other of a number of bacteria.